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# Evaluation of gum mastic (*Pistacia lentiscus*) as a microencapsulating and matrix forming material for sustained drug release

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ABSTRACT

In this study, a natural gum mastic was evaluated as a microencapsulating and matrix-forming material for sustained drug release. Mastic was characterized for its physicochemical properties. Microparticles were prepared by oil-in-oil solvent evaporation method. Matrix tablets were prepared by wet and melt granulation techniques. Diclofenac sodium (DFS) and diltiazem hydrochloride (DLTZ) were used as model drugs. Mastic produced discrete and spherical microspheres with DLTZ and microcapsules with DFS. Particle size and drug loading of microparticles was in the range of 22–62 μm and 50–87%, respectively. Increase in mastic: drug ratio increased microparticle size, improved drug loading and decreased the drug release rate. Microparticles with gum: drug ratio of 2:1 could sustain DLTZ release up to 12 h and released 57% DFS in 12 h. Mastic produced tablets with acceptable pharmacotechnical properties. A 30% w/w of mastic in tablet could sustain DLTZ release for 5 h from wet granulation, and DFS release for 8 h and 11 h from wet and melt granulation, respectively. Results revealed that a natural gum mastic can be used successfully to formulate matrix tablets and microparticles for sustained drug release.



## 1. Introduction

The merits of natural gums have been well acknowledged in the past many years; they are readily available, cost effective, eco-friendly, fairly degradable and biocompatible [1,2]. They can be modified and converted into useful semi-synthetic and synthetic materials for pharmaceutical applications [3]. The numerous natural gums such as agar, chitosan, guar gum, xanthan gum, locust been gum and sodium alginate have been

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used successfully for various pharmaceutical applications. Previously, we demonstrated that gum copal and damar can be used to prepare sustained release matrix tablets [2] and microparticles of water soluble and water insoluble therapeutic agents [4]. We have also shown that PEGylation of natural gum rosin yields derivatives having an excellent film forming ability for the drug delivery applications [3,5–7]. In view of this, it is apparent that natural gums and their derivatives are promising candidates to design the sustain drug delivery systems.

Gum mastic is a natural resin obtained from broad-leaved variety of *Pistacia lentiscus* (Family Anacardiaceae), which is a shrub or small tree of the *pistacio* genus growing up to 4 m tall and is cultivated for its aromatic resin [8]. Mastic tree is naturally distributed in areas that enclose the coastal regions of the Mediterranean, Portugal and tropical Africa and grows on all kinds of soil. Gum mastic is produced in the form of small tears that are pale yellow in color. The chief constituent of mastic is resin, which is associated with about 2% of volatile oil. The resin can be separated into the following constituents: α- and β-masticinic acids (together about 4% of the drug), masticolic acid (crystalline, traces), α- and β-masticonic acids (amorphous, about 38%), α-masticoresene (soluble in alcohol, about 30%), β-masticoresene (also called as masticin, insoluble in alcohol, about 20%). The volatile oil of gum mastic contains mostly the d-pinene [9]. Owing to its film-forming propensity, mastic has been used in the preparation of varnishes. Its age-long use in Arab countries was for chewing, where it sweetens the breath and helps preserve the teeth and gums [10]. As a medicinal agent, it has been used in the treatment of gastritis, gastroesophageal reflux diseases and intestinal infections [11]. It has also been evaluated as a crude drug for gastric and duodenal anti-ulcer activity [12]. It was found that mastic has specific antibacterial activity against *Helicobacter pylori* [13].

In the field of drug delivery system, gum mastic has been evaluated for its application in the enteric coating [14], film coating [15], matrix system [16], stability improvement [17,18] and controlled drug release [19–21]. However, all of these studies evaluated gum mastic in combination with either polymers, gums, film formers or matrix forming materials. Recently, Deshpande et al. [22] have shown that gum mastic has potential to produce controlled release spheroid by roller compaction technique. Since gum mastic is safe, well tolerated by humans, hydrophobic and has a film forming ability, it can be used to fabricate the sustained drug delivery devices. This study was thus undertaken with an objective to investigate gum mastic as a microencapsulating and matrix forming material for sustained drug release.

DFS is a non-steroidal anti-inflammatory agent that has been widely used to reduce pain and inflammation. Chemically, it is sodium 2-{2-[(2,6 -dichlorophenyl) amino] phenyl} acetate. Owing to its low solubility and high permeability, DFS has been classified as a BCS class 2 compound within the biopharmaceutics classification system. After oral administration, it is completely absorbed, however, due to the first-pass metabolism, only about 50% of the absorbed dose can be available systemically [23]. In addition, the terminal half-life of unchanged DFS is only about 2 h [23]. On the other hand, DLTZ is a calcium channel blocker that has been used in the prevention and long term treatment of angina pectoris and hypertension. It is a low molecular weight (450.99 Dalton) compound, which is soluble in water, methanol and chloroform. Because of the extensive first pass metabolism, oral bioavailability of DLTZ is approximately 40%, and the half-life is reported to be about 3–5 h [24]. The above details in particular suggest that DFS and DLTZ have low oral bioavailability and short biological half life, which make them suitable candidates for the sustained or controlled drug delivery systems.

## 2. Materials and methods

### 2.1. Materials

Gum mastic was received as a gift sample from M/s Innovative Marketing Services, Mumbai, India. DFS and DLTZ were received as gift samples from M/s Zim Laboratory Ltd., Nagpur, India. Microcrystalline cellulose (Avicel PH 101, FMC, Biopolymer) was received as a gift sample Signet chemical corporation Pvt., Ltd., India. Chloroform (Rankem), petroleum ether 60–80 (Ranbaxy), and heavy liquid paraffin (Rankem) were procured and used. All other chemicals were of analytical grade.

### 2.2. Characterization of gum mastic

Mastic was examined visually for appearance. Acid value was determined as per the method described in literature [25]. The softening and melting temperatures were determined using capillary tube, thermometer and Thiele tube. The solubility in different organic solvents and buffers was determined at 25 ± 1 °C. The MW and polydispersity were determined by the Gel Permeation Chromatography system (Perkin-Elmer) equipped with refractive index detector (La Chrom Detector L-7490). The glass transition temperature ($T_g$) was determined by the Differential Scanning Calorimetry (DSC, Mettler-Toledo Star System). The viscosity of 20% w/v solution in acetone was measured at 25 ± 1 °C by a Brookfield viscometer using spindle no. 4 (Brookfield Engineering Laboratories, Inc., Stoughton, Massachusetts).

### 2.3. Gum mastic microparticles

#### 2.3.1. Preparation of microparticles

Microparticles were prepared by oil-in-oil emulsion solvent evaporation method. Various microparticle compositions are summarized in Table 1. In brief, 1 g mastic was dissolved in 12 ml of dichloromethane. To this, drug powder and magnesium stearate (10% w/w of mastic weight) were added. Resulting dispersion was stirred on a magnetic stirrer for 5 min and emulsified into 150 ml of rotating liquid paraffin in a 250 ml of glass beaker. The above system was stirred (with stirrer blade position in the center of glass beaker) for 4 h at 40 ± 2 °C. As one of the variable, stirrer blade position was changed from center to bottom of the glass beaker. The microparticles were collected by vacuum filtration and washed two times with 25 ml of petroleum ether (60–80). The microparticles were stored in desiccators maintained at 0% relative humidity before further use.